Elective Surgery: Low Molecular Weight Heparin, Warfarin, Direct Oral Anticoagulant and Anti-Platelet Management Guidance

NHS Lothian

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Target Audience:	All staff members involved with adult elective surgery		
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Date	Author	Version/Page	Reason for change
Nov 2023	Dr Adam Paul, Consultant Anaesthetist Dr Julia Anderson, Consultant Haematologist Dr Andrew Page, Consultant Haematologist Reshma Chhana, Lead Clinical Pharmacist Katrina Yu, Lead pharmacist- haematology/ immunology	1	New guidance to support with warfarin, direct oral anticoagulant, and antiplatelet medication management for elective surgery
Nov 2024	Julia Anderson, Consultant Haematologist Katrina Yu, Lead pharmacist- haematology/ immunology	1.1 (Page 5)	Asterisk at the bottom of the page should refer to MINOR, rather than low bleeding risk

Dissemination Plan

Audience	Method	Paper/Electronic	Responsible staff member
All Staff	Upload – intranet & RightDecisions NHS Lothian App	Electronic	D&T/Consultant Haematologist
Surgical, Theatre & Anaesthetics, Gynaecology Staff	E-mail to all site relevant AMDs	Electronic	Consultant Haematologist
Pharmacists	E-mail / Site leads	Electronic	Lead Haematology Pharmacist
Thrombosis Committee	Discussed and circulated; including haem at HYCP	Electronic	Consultant Haematologist
All relevant medical staff	Electronic/verbal	Electronic	Theatre & Anaesthetics NHS Lothian Surgery Teams Gynaecology

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Contents

1.0 Introduction

This document provides generalised guidance for the management of warfarin, therapeutic low molecular weight heparin (LMWH), direct oral anticoagulant (DOACs) and anti-platelet (APT) in elective surgery. The decision to stop these high-risk medications before surgery and the timing of restarting afterwards reflects a balance between risk of surgical bleeding and the risk of a repeat event. Different surgical procedures hold varying bleeding risk, so an individualised approach is necessary with reference to local unit guidance. For example, operations and procedures involving bleeding into a confined space, such as neurosurgery, or procedures with high bleeding risk, require a more cautious re-introduction of anticoagulation.

2.0 Purpose & Scope

This document provides guidance for the management of warfarin, LMWH, DOACs and APT in elective surgery for adult patients. The decision to stop these high-risk medications before surgery and the timing of restarting afterwards reflects a balance between risk of surgical bleeding and the risk of a repeat event. Different surgical procedures hold varying bleeding risk, so an individualised approach is necessary.

This guidance does not cover emergency surgery, and any anticoagulation therapy in emergency surgery should be addressed according to individual risk factors, with consideration using existing emergency reversal protocols, and at the discretion of the surgeon. This guidance is not to be used for pregnant patients.

3.0 Definitions

DOAC – direct oral anticoagulant

CrCl – creatinine clearance

SC – subcutaneous

VTE – venous thromboembolism

AF – atrial fibrillation

MHV – mechanical heart valve

PCI – percutaneous coronary intervention

APT – anti-platelet

INR – international normalised ratio

LMWH – low molecular weight heparin

CVA – cerebral vascular accident

TIA – transient ischaemic attack

ACS – acute coronary syndrome

FBC – full blood count

4.0 Roles and responsibilities

Operating surgeon – to define the bleeding risk posed to the patient for the operation and how quickly anticoagulation is to be introduced post-operatively. To ensure thrombotic risks associated with perioperative cessation of anticoagulation are discussed with the patient and understood.

5.0 Main content

KEY MESSAGES:

- A written pre-operative management plan, based on this guidance, should be available in the *Correspondence and/or Clinical Notes* section on TRAK for the multidisciplinary team to refer to.
- Re-escalation of anticoagulation is dependent on the bleeding risk of surgery. For very high bleeding risk (e.g. neurosurgery) situations seek advice from Haematology or follow unit-specific protocol.
- Within 3 months of an episode of VTE, TIA or stroke consider postponement of elective surgery.
- Do not withhold dual antiplatelet therapy in patients with recent acute coronary syndrome (ACS) or recent percutaneous coronary intervention (PCI).

The table below outlines bleeding risks of common procedures including those where anticoagulation therapy may not need to be interrupted. This is intended as a guide rather than a comprehensive list of the bleeding risks for all operations. The operating surgeon best defines the exact bleeding risk of the procedure, and impact of bleeding (i.e. bleeding in neurosurgery is of high impact); the operating surgeon should be consulted to confirm the need for anticoagulation interruption.

Minor Bleeding Risk*
Dental surgery (simple 1-3 extractions, abscess incision)
Cataract of glaucoma intervention
Endoscopy without resection or biopsy
Superficial surgery (e.g. Abscess excision, simple skin biopsy)
Low Bleeding Risk (Bleeding infrequent or of low clinical impact)
Endoscopy with biopsy
Prostate or bladder biopsy
Pacemaker or ICD implantation
Biliary or pancreatic stenting
Device-assisted enteroscopy without polypectomy
High Bleeding Risk (Bleeding frequent and/or of high impact)
Complex endoscopy (e.g. polypectomy, ERCP with sphincterotomy etc.)
Spinal or epidural anaesthesia: lumbar diagnostic puncture
Thoracic surgery
Abdominal surgery
Major Orthopaedic surgery
Liver biopsy
Transurethral prostate resection
Kidney biopsy

**It is often possible to perform minor bleeding risk procedures without interrupting anticoagulation therapy – this will be dependent on the INR for warfarin and ensuring prudent timing of the procedure in relation to DOAC administration time*

5.1 Warfarin

Patients are prescribed long term warfarin to reduce the lifetime risk of stroke, transient ischaemic attack (TIA) or venous thrombo-embolism (VTE).

For a patient prescribed warfarin after a **recent** (defined as within 3 months) stroke, TIA or VTE, consider postponing **elective** surgery for three to six months. *****PLEASE NOTE THIS IS A HIGH-RISK SITUATION - SEEK ADVICE FROM THE DUTY HAEMATOLOGIST *****

Risk stratification: thrombosis risk

If none of the indications in the "increased risk / consider bridging" column apply. The patient has a low risk of thrombosis and bridging is not necessary

Indication for warfarin	**The patient is at INCREASED risk of thrombosis and bridging should be CONSIDERED if any of the following apply:**
Venous thrombo-embolism (VTE)	1. Patient has had VTE in the last three months [1] 2. Patient has previously had VTE whilst on therapeutic anticoagulation 3. Patient has a target INR ≥ 3.5 Patient with VTE event with underlying high risk medical condition e.g. myeloproliferative disorder
Atrial Fibrillation (AF)	1. Patient has had stroke or TIA in the last three months[1]. 2. Patient has had a previous stroke or TIA (at any time) and three or more of the following risk factors: - Hypertension - (>140/90 mmHg or on antihypertensives) - Age >75 years - Diabetes mellitus - Severe LV impairment[2]
Mechanical Heart Valve (MHV)	1. All patients with mechanical mitral valve 2. All patients with mechanical aortic valve **and** any of: - Atrial fibrillation - Starr Edwards (Ball & Cage) prosthesis[3] - Severe LV impairment [2] - Stroke/TIA in last six months [4]
Cerebral Vascular Accident or Transient Ischaemic Attack (CVA/TIA)	1. Patient with CVA/TIA in last 3 months 2. Patients with previous CVA/TIA and 3 or more of the following a. Congestive cardiac failure b. Hypertension (BP>140/90mmHg or on antihypertensive treatment) c. Age >75 years d. Diabetes mellitus

[1] ***VERY HIGH RISK:*** *if possible postpone elective surgery until at least 3 months after event.*
[2] *If cardiac function has not been documented there is no need to perform echocardiography to access need for bridging unless there is a clinical concern about congestive cardiac failure.*
[3] *This type of valve was not implanted after 1993.*
[4] ***VERY HIGH RISK:*** *if possible postpone elective surgery until at least 6 months after event.*

Management of warfarin before and after surgery

Before surgery
Can surgery proceed without stopping warfarin? *i.e. some patients undergoing dental extraction, cataract surgery, simple biopsy procedures or where the operation site is easily compressed.*
If not known, check with patient's surgeon.

- If warfarin is to be stopped before surgery, the last dose should be taken on Day minus 6 (where "Day 0" is date of surgery).
- Further management is guided by risk stratification
  - Patients at **increased** risk of thrombosis may require peri-operative therapeutic anticoagulation ("BRIDGING") with LMWH i.e. dalteparin.
  - Patients at **low** risk of thrombosis may simply stop warfarin. The need for peri-operative *prophylactic* dalteparin is determined by the usual VTE risk assessment criteria.

	Increased Risk of Thrombosis	**Low Risk of Thrombosis**
Day minus 6	Take last dose of warfarin	Take last dose of warfarin
Day minus 5	No warfarin	No warfarin
Day minus 4	No warfarin	No warfarin
Day minus 3	Check INR; if INR <2 commence *therapeutic** dose dalteparin** (No warfarin)	No warfarin
Day minus 2	Continue *therapeutic** dose dalteparin** (No warfarin)	No warfarin
Day minus 1	*Prophylactic* dose dalteparin** *(Adjust for low body weight <50kg, seek haematology advice if >150kg) (No warfarin)*	No warfarin
Day 0 = day of procedure	Check INR pre-operatively	Check INR pre-operatively.
	No dalteparin/ warfarin before surgery. Prophylactic dalteparin 8-12 hours after end surgery (if no issues with haemostasis, directed by surgeon).***	

* 200 units / kg, max 18,000 units sub cut once daily and CrCl > 30 ml/min. If CrCl <30ml/min, seek advice from haematology. (*CrCl Calculator link: http://intranet.lothian.scot.nhs.uk/Directory/AMT/Documents/Creatinine_Clearance_Calculator_Version1.xlsx*)
(may also be given twice daily – i.e. 100 units / kg twice daily, which may be more effective in patients at particularly high risk of thrombosis, such as mechanical heart valves)
** Before 18:00h.

***For a patient with a body weight of 50-100kg, start dalteparin 5000 units sub cut once daily 8-12 hours after surgery at discretion of Consultant Surgeon followed by dalteparin 5000 units daily from post op day +1. If body weight less than 50kg, the dose is dalteparin 2500 units sub cut once daily. If body weight is over 100kg follow unit specific protocol (because dosing depends on bleeding risk of surgery)

After surgery ("standard bleeding risk")
Definition: "Day 1" = the first day after surgery, if haemostasis has been secured (as directed by the operating surgeon)

Restart warfarin at the patient's usual maintenance dose as soon as the risk of post-op bleeding is acceptable. INR should be checked daily from post-op day +2 of warfarin treatment if an in-patient.
For operations and procedures involving bleeding into a confined space, such as neurosurgery, or procedures with high bleeding risk, a more cautious re-introduction of anticoagulation is necessary.

	Increased Risk of Thrombosis	Low Risk of Thrombosis
Days 1 & 2	Warfarin: at patient's usual dose Dalteparin: prophylactic*** dose (not for therapeutic dosing until at least 48-72 hours post-op due to increased bleeding risk).	Warfarin at patient's usual dose Dalteparin: prophylactic dose
Days 3 & 4	Warfarin at patient's usual dose. Dalteparin, either: Intermediate dose (i.e. *prophylactic* dose 12 hourly) **or** start *therapeutic** dose	Continue warfarin at patient's usual dose Continue prophylactic dalteparin until INR is patient's usual therapeutic range *i.e. >2 (if INR range is 2-3) (or 2.5 if target range is 2.5-3.5)* If the oral route is not available by day 3 consider following the Increased Risk pathway
Day 5	Warfarin at patient's usual dose. If not already done or INR subtherapeutic: start *therapeutic** dalteparin	
Day 6 onwards	Warfarin at patient's usual dose. Continue therapeutic dalteparin until INR is >2 (if INR range is 2-3)	

INR should be checked daily in all in-patients taking warfarin until it is in the patient's therapeutic range

For patients being discharged home, the INR should be checked on the third day after restarting the patient's usual maintenance dose of warfarin. Prophylactic dalteparin should be continued until INR is >2 or within the patients therapeutic range *i.e. 2.5 if target range is 2.5-3.5*. If this falls over a weekend the patient will need to attend the parent ward for INR check.

* 200 units / kg, max 18,000 units and CrCl > 30 ml/min. If CrCl <30ml/min, haematology must be contacted. (*CrCl Calculator link: http://intranet.lothian.scot.nhs.uk/Directory/AMT/Documents/Creatinine_Clearance_Calculator_Version1.xlsx*)
(may also be given twice daily - ie 100 units / kg twice daily, which may be more effective in patients at particularly high risk of thrombosis)
** Before 18:00h.
*** For a patient with a body weight of 50-100 kg, start Dalteparin 5000 units SC once daily 8-12 hours after surgery at the discretion of the consultant surgeon followed by 5000 units daily from post-op day +1. If body weight <50kg, the dose should be 2500 units SC once daily.

5.2 Direct Oral Anticoagulants (DOACs)

Examples of direct oral anticoagulants are apixaban, dabigatran, rivaroxaban and edoxaban. Advantages of DOACs compared with warfarin and heparin are a predictable dose response, fewer drug-drug interactions and oral administration. On the other hand, they accumulate in patients with renal impairment and monitoring tests for measuring their anticoagulant activity are not widely available. **Bridging with therapeutic LMWH is not required for patients on a DOAC due to the predictable pharmacokinetics allowing for properly timed short-term cessation prior to surgery, except if acute thrombosis within 3 months and /or patient has eGFR less than 45ml/min when a switch to pre-operative LMWH may be indicated**.

Guidance on the management of DOACs at the time of elective surgery is based on an estimation of the drug's half-life and thus its persistence in the circulation (taking into account renal function), combined with the bleeding risk of the proposed procedure.

- Most operations should be classified as "high bleeding risk".
- For operations and procedures for which warfarin would be continued consider classifying as "low bleeding risk".
- "Day 0" is the day of surgery; assume the patient is on the morning list

Management of DOACs before surgery:

Direct Oral Anticoagulants (DOACs)			When to stop before surgery	
	CrCl (ml/min)	Estd half-life (hours)	Low bleeding risk *	High bleeding risk or Spinal or epidural anaesthesia is likely
Apixaban	>30	8	24h, last dose on evening of day minus 2	48h, last dose on evening of day minus 3
	<30		48h, last dose on evening of day minus 3	72 h, last dose on evening of day minus 4
Dabigatran	≥50	15	24h, last dose on evening of day minus 2	48h, last dose on evening of day minus 3
	30 to 49	18	72h, last dose on evening of day minus 4	96h, last dose on evening of day minus 5
Rivaroxaban¥	>30	9	24h, last dose day minus 2	48 h, last dose day minus 3
	<30		48h, last dose day -3	72h, last dose day minus 4
Edoxaban	>30	10-14	24h, last dose day -2	48h, last dose day minus 3
	<30		48h, last dose day -3	72h, last dose day minus 4
*e.g: superficial operations, procedures for which warfarin would be continued.				

Note: ¥peri-operative cessation of low-dose rivaroxaban (2.5mg twice daily) has not been studied and patients should be managed on a case-by-case basis by discussing arterial thrombotic risk with a cardiologist or vascular surgeon.

Restarting DOAC after surgery

DOACs are well absorbed orally and reach peak anticoagulant levels a few hours after ingestion. With the exception of elective hip and knee arthroplasty*, use of prophylactic doses of LMWH may be considered post-operatively if the patient is unable to recommence the DOAC within 24 hours of surgery due to potential bleeding risks associated with surgery/procedure or inability to take oral therapy. Commencement of LMWH should be based on thrombosis risks vs associated bleeding risks as highlighted earlier.

Procedure Risk	Post-operative advice
Minor/low risk procedures	Once haemostasis has been fully secured, DOAC can be recommenced within 8-12 hours post-operatively
High risk procedure / increased bleeding risk	Do not recommence at full-dose until at least 48-72 hours post-op *Can consider prophylactic LMWH 8-12 hours post-op based on thromboembolic and bleeding risks*
Very high bleeding risk/potential to bleed into confined space	Consider no earlier than 5-7 days post-operatively
Prophylactic LMWH should be discontinued immediately on recommencing the DOAC	

* Rivaroxaban 10mg once daily, and Apixaban 2.5mg twice daily are licensed for use in thromboprophylaxis in elective hip and knee arthroplasty, and the instructions for use followed as set out by the manufacturer in terms of timing of initiation.

5.3 Therapeutic low-molecular-weight heparin (LMWH) before & after scheduled surgery (normal renal function)

Essential information: body weight (kg), FBC and creatinine clearance, and confirm time of administration of LMWH*
http://intranet.lothian.scot.nhs.uk/Directory/AMT/Documents/Creatinine_Clearance_Calculator_Version1.xlsx
If Cr Cl less than 45 ml/min then seek advice from haematology

**If therapeutic dalteparin is usually taken at 1800hrs or later, then no need for prophylactic dose on day minus 1 (i.e no anticoagulation is required on day minus 1)*

· **Check indication for anticoagulation: was VTE over 3 months ago?** ***If less than 3 months ago seek advice from haematology as this is a high-risk situation****

· **Check patient on correct dose of dalteparin 200 units/Kg SC once daily, max 18000 units and the time of administration**

Note: oncology patients might be on dalteparin 150 units/kg SC once daily if the patient is over 1 month post diagnosis of venous thromboembolism (can use this guidance but seek advice from haematology in case the dose of dalteparin needs adjusted back to full therapeutic dose pre-operatively).

Note: if any other LMWH brand, or regimen (e.g. twelve hourly dosing in obese patients) is in use, this guidance is not relevant. Seek advice from haematology

Note: the re-escalation regimen is at the discretion of the attending surgical team

	High risk of thrombosis "standard risk of bleeding"	**Any thrombotic risk, but Increased risk of bleeding/ consequences of bleeding (e.g. neurosurgery)**
Before surgery		
Day minus 3	Take therapeutic Dalteparin as usual	Take last dose of therapeutic Dalteparin
Day minus 2	Take last dose of therapeutic Dalteparin	No Dalteparin
Day minus 1	Prophylactic dose of Dalteparin before 18:00h*	No Dalteparin
**If therapeutic Dalteparin is usually taken at 1800hrs or later, then there is no need for a prophylactic dose on day minus 1 (i.e no anticoagulation is required on day minus 1)*		
Day 0 = day of procedure	No Dalteparin before operation; Prophylactic Dalteparin 8-12 hours after surgery if no issues with haemostasis	No Dalteparin before operation; Mechanical measures (TEDs and flowtron boots) after surgery
After surgery		
If an epidural catheter is in situ post-operatively, then only standard weight-based prophylaxis can be given until the catheter is removed (usually post-op day 2), and prescribing is at the discretion of the Pain Team and anaesthetist.		
Day 1 + 2	Prophylactic Dalteparin	Mechanical measures (TEDs and flowtron boots) Prophylactic Dalteparin at discretion of surgeon
Day 3	Intermediate dose Dalteparin (i.e. prophylactic dose 12 hourly) or therapeutic Dalteparin, at discretion of surgeon	Prophylactic Dalteparin at discretion of surgeon
Day 4	Intermediate dose Dalteparin (i.e. prophylactic dose 12 hourly) or therapeutic Dalteparin, at discretion of surgeon	Prophylactic Dalteparin
Day 5	Therapeutic Dalteparin	Prophylactic Dalteparin
Day 6	Therapeutic Dalteparin	Prophylactic Dalteparin
Day 7	Therapeutic Dalteparin	Depending on surgery, consider Intermediate dose Dalteparin (i.e. prophylactic dose 12 hourly) continuing days 7-14 or longer, prior to re-introducing therapeutic anticoagulation

5.4 Anti-platelet medication

Anti-platelet drugs are used in the secondary prevention of cardiovascular disease. Examples include clopidogrel after stroke or TIA and dual antiplatelet therapy with aspirin plus (most commonly) clopidogrel after acute coronary syndromes (ACS) and particularly after coronary stenting.

If a patient is on dual anti-platelet therapy, please discuss with the consultant anaesthetist.

Dual anti-platelet therapy after ACS or coronary stenting should not be stopped without discussion with the patient's cardiologist THIS IS DEEMED A HIGH-RISK SITUATION

Anti-platelet drug	Time to peak effect on coagulation	Elimination half life	When to stop before surgery
Non-steroidal anti-inflammatory drugs (NSAIDs)	1 – 12 hours	1 – 12 hours	Continue[1] (***see note below***) For high-bleeding risk surgery, long-acting NSAIDs should be stopped[2]
Dipyridamole	75 min	10 hours	Continue[1] (***see note below***), unless also taking another anti-platelet drug
Aspirin *(low-dose ≤150mg)*	12 – 24 hours	Irreversible effect	Continue[1] (***see note below***)
Clopidogrel	12- 24 hours	Irreversible effect	7 days (last dose day minus 8)
Prasugrel	15 – 30 min	Irreversible effect	7 days (last dose day minus 8)
Ticagrelor	2 hours	8 – 12 hours	5 days (last dose day minus 6)
Dual antiplatelets: aspirin + $P2Y_{12}$inhibitor *i.e. clopidogrel, prasugrel, ticagrelor)*	*As above*	*As above*	Low bleeding risk: continue both Moderate bleeding risk: continue aspirin and withhold $P2Y_{12}$inhibitor as above

1 In the following circumstances (see bullet points below), as these antiplatelet drugs remain in the circulation and affect transfused platelets, aspirin, dipyridamole and non-steroidal anti-inflammatory drugs (NSAIDs) (short-acting) should be ***withheld*** *as per the table below:*

- *If a platelet transfusion is required and/or major blood loss is a possibility*
- *For those procedures associated with high risk of bleeding or bleeding complications (e.g. spinal surgery, certain ophthalmological and neurosurgical procedures)*
- *For individuals who refuse blood transfusion for religious reasons e.g. Jehovah's Witness.*

The following medications should be **withheld**:

NSAIDs (short-acting)	*Withhold on day of surgery*
Dipyridamole	*Stop day before surgery*
Aspirin	*Stop 7 days pre-operatively*

Advice regarding longer acting NSAIDs on next page (page 14)

Longer acting NSAIDs

[2] Longer acting NSAIDs are listed below. Their anti-platelet effect does not warrant withholding routinely before surgery, but they may need to be withheld in patients at increased risk of post-operative renal dysfunction and/or any additional raised bleeding risk:

Long-acting NSAIDs		
Name of Drug	**Half-life (hours)**	**Time to stop pre-operatively (days)**
Etodolac MR	Approx. 7	2
Indomethacin	2 – 11	3*
Ketoprofen MR	8	2
Nabumetone	Approx. 24	5
Naproxen	12 – 15	4
Piroxicam	50	11
Sulindac	16 – 18 **	4
Tenoxicam	72	15

Restarting anti-platelet medication after surgery

Anti-platelet medication may be restarted after surgery as soon as the bleeding risk is considered acceptable and the oral route is available and should be given alongside dalteparin thromboprophylaxis for venous thrombosis.

6.0 Associated materials

7.0 Evidence base/references

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8.0 Stakeholder consultation

Consultation
Thrombosis Committee
Anaesthetic Group
Drugs & Therapeutics Committee
Surgical Consultant Group
Pharmacy Teams

9.0 Monitoring and review

Element (s) to be monitored	Person (position) responsible for the monitoring	Method	Monitoring frequency	Committee or group monitoring is reported to including responsibility for action plans and changes in practice
SAER / Datix	*Thrombosis Committee*	*Review by committee members*	*Quarterly*	*Thrombosis Committee*